**Remarks**

Pursuant to the Office Action of July 23, 2002, Applicants amended claims 90, 92, 97, and 117

In the Office Action of July 23, 2002, the Examiner rejected claims 90, 92-94, 96 and 117 under 35 USC (102(b) as anticipated by US Patent 4,676,274 to Brown. The Examiner rejected claims 91, 98 and 99 under 35 USC 103(a) as obvious over US Patent 4,676,274 to Brown, and rejected claim 95 under 35 USC 103(a) as obvious over US Patent 4,676,274 to Brown in view of US Patent 5,589,350 to Bochner, and also rejected claims 101-116 and 118-131 under 35 USC 103(a) as obvious over US Patent 4,676,274 to Brown in view of US Patent US 5,498,392 to Wilding et al. Particularly in view of the above amendments, Applicants respectfully disagrees with these rejections.

As claimed in claim 90, the invention is a method of repeatedly measuring a known volume of a fluid in a miniature fluidic system. The method includes providing a microfabricated device having at least first and second chambers connected by at least one channel disposed therein, wherein the at least first and second chambers are in fluid connection, each comprise at least one vent port, and wherein at least one of the chambers is a volumetric chamber having a known volume. The method also includes providing a diaphragm valve for displacing fluid; filling the volumetric chamber with the fluid to create a first aliquot of the fluid; transporting the first aliquot of the fluid to the at least second chamber; and repeating the filling and transporting steps by applying pressure from an external source.

Neither Brown alone or in combination with Bochner or Wilding do not disclose this invention. Specifically, these reference do not disclose the above-recited combination including the miniature fluidic system with a diaphragm valve used to displace or transport fluid by applying pressure from an external source. Therefore, claim 90 is patentable over the cited references.

As claimed in claim 92, the invention is a method of measuring and processing a known volume of a fluid in a miniature fluidic system for integrated nucleic acid analysis.

The method includes the acts of providing a microfabricated device having at least first and second chambers disposed therein, wherein the first and second chambers include at least one vent port and at least one of the chambers is a volumetric chamber having a known volume. The method includes the acts of providing a sealable closure inlet to the microfabricated device, and providing at least one valve controlled by an external pressure source. The invention includes filling the volumetric chamber with the fluid to create a first aliquot of the fluid; opening the controllable valve; and transporting the first aliquot of the fluid to the at least second chamber by applying pressure from the external source.

Neither Brown alone or in combination with Bochner or Wilding do not disclose this invention. Specifically, these reference do not disclose the above-recited combination including the miniature fluidic system including a sealable closure inlet (for example, using a septum claimed in claim 134) to the microfabricated device used to input a liquid from an external source. Therefore, claim 92 is clearly patentable over the cited references.

As claimed in claim 117, the invention is a miniature fluidic system for measuring and processing a known volume of a fluid controlled by an external pressure source. The miniature fluidic system includes a microfabricated device having at least first and second chambers disposed therein, the first and second chambers including at least one vent port and at least one of the chambers being a volumetric chamber having a known volume; and there is a sealable closure inlet to the microfabricated device constructed to enable introduction of a liquid. The system also includes at least one valve controlled by an external pressure source; means for filling the volumetric chamber with the fluid to create a first aliquot of the fluid; means for opening the controllable valve; and means for transporting the first aliquot of the fluid to the at least second chamber.

Neither Brown alone or in combination with Bochner or Wilding do not disclose this invention. Specifically, these reference do not disclose the above-recited system including the miniature fluidic system having a sealable closure inlet (for example, a

septum recited in claim 135) to the microfabricated device used to input a liquid from an external source. Therefore, claim 117 is clearly patentable over the cited references.

In summary, independent claims 90, 92, and 117 are patentable as explained above. Dependent claims 91, 93 through 116, and 118 through 135 include additional novel combinations of features. Therefore, all pending claims are now in condition for allowance, and such action is respectfully requested.

Regarding the obviousness-double patenting rejection, in U.S. Patent Application 08/671,928, filed on June 27, 1996 (U.S. Patent 5,922,591) the Examiner made a restriction requirement dividing the filed claims into four groups including Group IV (claims 90 and 91). In this application, Applicants pursued only the claims directed to Group IV, whereas in U.S. Patent 6,197,595 Applicants pursued only the claims directed to Group II. Therefore, the obviousness-double patenting rejection should be withdrawn.

Should there be any outstanding issue left, the Examiner is respectfully invited to call the undersigned to resolve such issues.

Please charge all PTO fees and apply all credits to the Deposit Account No. 01-0431.

Respectfully submitted,

Ivan D. Zitkovsky, Reg. No. 37,482
6 Freeman Circle
Lexington, MA 02421-7713

Tel. +781-943-4012 (or 274-8064)
Fax +781-274-8065

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The undersigned hereby certifies that this document is being placed in the United States mail with first-class postage attached, addressed to Commissioner for Patents, Washington, D.C. 20231, on

November 25, 2002

Ivan D. Zitkovsky

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

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|---|---|---|---|
| Applicant: | ROLFE C. ANDERSON et al. | Examiner: | W. Beisner |
| Serial No: | 09/751,658 | Art Unit: | 1744 |
| Filed: | December 31, 2000 | | |
| For: | INTEGRATED NUCLEIC ACID DIAGNOSTIC DEVICE | | |

**AMENDMENTS**
(With changes shown)

90. (Twice Amended) A method of repeatedly measuring a known volume of a fluid in a miniature fluidic system, comprising:

providing a microfabricated device having at least first and second chambers connected by at least one channel disposed therein, wherein said at least first and second chambers are in fluid connection, each comprise at least one vent port, and wherein at least one of said chambers is a volumetric chamber having a known volume;

providing a diaphragm valve for displacing fluid;

filling said volumetric chamber with said fluid to create a first aliquot of said fluid;

transporting said first aliquot of said fluid to said at least second chamber; and

repeating said filling and transporting steps by applying pressure from an external source.

92. (Amended) A method of measuring and processing a known volume of a fluid in a miniature fluidic system for integrated nucleic acid analysis, comprising the acts of:

providing a microfabricated device having at least first and second chambers disposed therein, said at least first and second chambers including at least one vent port and at least one of said chambers being a volumetric chamber having a known volume;

providing a sealable closure inlet to said microfabricated device;

providing at least one valve controlled by an external pressure source;

filling said volumetric chamber with said fluid to create a first aliquot of said fluid;

opening said controllable valve; and

transporting said first aliquot of said fluid to said at least second chamber by applying pressure from said external source.

97. (Amended) The method of claim 96 [97] wherein said using said pneumatic system includes using a differential pressure delivery system capable of applying a first pressure to said volumetric chamber and a second pressure to said second chamber.

117. (Amended) A miniature fluidic system for measuring and processing a known volume of a fluid controlled by an external pressure source, comprising:

a microfabricated device having at least first and second chambers disposed therein, said at least first and second chambers including at least one vent port and at least one of said chambers being a volumetric chamber having a known volume;

a sealable closure inlet to said microfabricated device constructed to enable introduction of a liquid;

at least one valve controlled by an external pressure source;

means for filling said volumetric chamber with said fluid to create a first aliquot of said fluid;

means for opening said controllable valve; and

means for transporting said first aliquot of said fluid to said at least second chamber.

127. (Amended) The system of claim 117 wherein said sealable closure inlet is constructed for introduction of [fluid includes] a reagent.

128. (Amended) The system of claim 117 wherein sealable closure inlet is constructed for introduction of [fluid includes] a buffer.

129. (Amended)The system of claim 117 wherein sealable closure inlet is constructed for introduction of [fluid includes] a biological polymer.

130. (Amended) The system of claim 117 including means for reconstituting a reagent kept in a lyophilized form.

131. (Amended) The system of claim 130, wherein said means for reconstituting includes means for transporting said first aliquot of said fluid to said second chamber wherein said reagent is located.